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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/752,292	12/28/2000	Alex Chenchik	CLON-017US2	6642

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Bret Field
BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025

EXAMINER	
ZITOMER, STEPHANIE W	
ART UNIT	PAPER NUMBER
1634	

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8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/752,292	Applicant(s) CHENCHIK ET AL.	
	Examiner Stephanie Zitomer	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-10,12,13,15,16,18-22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-10,12,13,15,16,18-22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Application status

1. Receipt of the amendments filed April 12, 2002 is acknowledged.

2. All rejections applied in the previous Office action, paper no. 5, mailed January 29, 2002, have been withdrawn in view of the amendments to the claims, applicant's arguments and new grounds of rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

3. Claims 1, 4-10, 12, 13, 15, 16 and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The claims lack antecedent for "said at least one analyte/tagged affinity ligand complex" at claim 1 (a), line 2. It is suggested to delete "said".

(b) Claims 1 and 16 are confusing due to typographical errors: the word "as" at line 2 of claim 1(a) should be --at-- and the word "sold" at line 2 of claim 16(a) should be --solid--.

(c) Claims 7 and 15 lack antecedent basis in depending from a canceled claim. It is suggested to change the dependency.

Rejection under 35 U.S.C. 102(b): Anticipation

4. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by the patent to Brenner (5,863,722 issued January 26, 1999). Brenner discloses the claimed method of detecting at least one analyte in a sample comprising (a) forming a population of complexed analyte/tagged affinity ligands wherein the tag is an oligonucleotide (nucleic acid); (b) capturing the complexes on a solid support by hybridizing the tags with tag complements attached to the solid support (column 2, line 66-column 3, line 6; column 3, lines 45-65); and (c) detecting the presence of at least one analyte (column 3, lines 61-65).

Rejection under 35 U.S.C. 102(e): Anticipation

5. Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by the patent to Kamb et al. (6,060,240 filed December 13, 1996). Kamb et al. disclose the claimed method

of detecting at least one analyte in a sample comprising (a) forming a population of complexed analyte/tagged affinity ligand wherein the tag is an oligonucleotide (nucleic acid); (b) capturing the complexes on a solid support by hybridizing the tags with tag complements attached to the solid support (column 42, claim 22 incorporating claims 21, 13 and 6); and (c) detecting the presence of at least one analyte (column 6, lines 7-8).

Rejections under 35 U.S.C. 103(a): Obviousness

6. Claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner or Kamb et al. as applied to claim 1 above (paragraphs 4 and 5, respectively), and further in view of Shannon et al. (6251,588) and Lockhart et al. (6,333,155). The claim 1 method embodiments of claims 4-9 differ from that of Brenner wherein any difference in hybridization efficiency between any two tag/tag complements does not exceed about 10 fold (claim 4), about 5 fold (claim 5) or about 3 fold (claim 6) and wherein the level of cross-hybridization of any tag employed in the method does not exceed about 10% (claim 7), about 2% (claim 8) or about 1% (claim 9). However, the practice of optimizing hybridization efficiency and reducing background by minimizing cross-hybridization in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Furthermore, Brenner discusses the cross-hybridization problem at length and presents an algorithm for determining minimally cross-hybridizing nucleotide sets (column 6, line 13-column 7, line 45) and Kamb et al. also discuss designing sequences so as to minimize cross-hybridization (column 15, line 51-column 16, line 27). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal

differences and minimal cross-hybridization for the known benefits of minimizing interferences and maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

7. Claims 10, 12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb et al. as applied to claim 1 above (paragraph 5 and further in view of Burmer (6,087,103 filed March 4, 1998). The claimed invention method embodiments of claims 10, 12 and 15 differ from the method of Kamb et al. wherein the analyte is a polypeptide (claim 10) or proteins (claim 15) and the tagged affinity ligands comprise an antibody or binding fragment thereof (claim 12). However, in a method of detecting the presence of at least one analyte in a sample comprising contacting the sample with a population of tagged affinity ligands, Burmer teaches the embodiments wherein the analytes are polypeptides or proteins and wherein the ligand is an antibody (column 4, lines 66-67; column 7, lines 14-19). It would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to employ the tagged antibody ligand and polypeptide analyte of Burmer in the claim 6 method of Kamb et al. for the known benefit of directly comparing relative amounts of the expression products of the nucleic acids thereby determining changes during propagation of the host cell populations which may not have been reflected in the nucleic acid measurements. Regarding claim 13 wherein the tagged affinity ligands are labeled, Burmer teaches this embodiment (column 13, lines 7-8).

8. Claims 16, 18-22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb et al. as applied to claim 1 above (paragraph 5) in view of Lockhart and Shannon, cited above (paragraph 6), Burmer, cited above (paragraph 7), and further in view of Brown et al. (Nat. Gen. Suppl. 21:33-37, Jan. 1999). Regarding claim 16, the claimed invention differs from Kamb et al. wherein the array of distinct tag complements immobilized on a solid support, a set of affinity ligands comprising tags that hybridize to tag complements on the array and means for detecting the location of hybridized tag/tag complements comprise a kit. Kamb et al. disclose the array of distinct tag complements on a solid support having spatially discrete regions (column 5, lines 63-66; column 9, lines 32-

35; column 11, lines 2-7; column 14, lines 26-28) and a set of distinct tagged affinity ligands (column 17, lines 15-28 and 62-65). The claimed invention differs from Kamb et al. wherein these reagents comprise a kit. However, Burmer teaches a kit comprising similar reagents (column 15, lines 9-13). It would have been obvious and the skilled practitioner in the art would have been motivated to provide the reagents disclosed in Kamb et al. in kit form as taught by Burmer for the known benefits of convenient use and commercial application.

Regarding claim 22, the claimed array of distinct tag complements wherein at least one is hybridized to a tagged affinity ligand is disclosed by Kamb et al. (column 42, claim 22 incorporating claims 21 and 13).

Regarding claims 18, 19 and 22, the kit and array embodiments differ from Kamb et al. in view of Burmer wherein the magnitude of difference in hybridization efficiency between any two tag/tag complement pairs does not exceed about 10 fold and any tag in the set of tagged affinity ligands has a level of cross-hybridization with respect to the array that does not exceed 10%. However, the practice of optimizing hybridization efficiency and minimizing cross-hybridization in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefit of maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

Regarding claims 20 and 21, the claimed invention kit differs from that of Kamb et al. in view of Burmer wherein the means for identifying the physical location on the array comprises a medium that includes identifying information or a means for remotely assessing the information is provided in the kit wherein the latter is a website address. However, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to include printed information such as a website address in the kit in view of routine practice in the art of accessing public nucleotide sequence databases for sequence searching as taught by Kamb et al. (column 27, line 61-column 28, line 31) for the obvious benefit of obtaining a large amount of sequence information in a readily available format. For example, Brown et al. teach that the use of molecular arrays generates a large amount of information which may be managed and published via websites.

Regarding claim 24, the claimed invention array differs from that of Kamb et al. wherein the array has a density that does not exceed about 400 spots/square cm. However, oligonucleotide arrays routinely used in the prior art were known to have densities ranging from less than 100 to more than 1000 spots per square cm. Therefore, one of ordinary skill in the art at the time the claimed invention was made would have been motivated according to personal preference to select an array density appropriate to particular experimental parameters for the obvious benefit of optimizing results.

Provisional double patenting obviousness-type rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 4-9, 13, 15, 16, 18-22 and 24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7-13, 15-19 and 22 of copending Application No. 09/752,293. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matter, hybridization assays on arrays via nucleic acid tag/tag complements, is the same in both sets of claims. The '292 claims are generic to those of the '293 application wherein the '292 claims encompasses the particulars of the '293 claim 1 wherein such assays were routinely practiced in the art without the particulars of gene-specific generation of target nucleic acids. Additional embodiments of the assay method are the same in both application claim sets.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Prior art of interest

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Rothberg et al. (WO 99/28505) provides an example in the prior art of the concept and use of "universal arrays". The publication discloses a "universal detection array" comprising capture tags which are complementary to an "additional sequence" in each of the analyte nucleic acids.

Conclusion

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact Patent Analyst Tiffany Tabb at 703-605-1238.

S Zitomer
Stephanie Zitomer, Ph.D.
June 12, 2002